UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MICHEL SADELAIN, NAI-KONG V. CHEUNG, ANJA KRAUSE and HONG-FEN GUO

Appeal No. 2004-1930
Application No. 08/940,544

HEARD: March 15, 2005

Before WILLIAM F. SMITH, MILLS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2, 6 and 7.[1] Claim 1 is representative of the subject matter on appeal, and reads as follows:

> 1. A recombinant polynucleotide encoding a fusion protein, wherein the fusion protein comprises
>
> (a) a single chain antibody comprising the variable region of a light chain of a selected antibody and the variable region of the heavy chain of the selected antibody;
>
> (b) the signaling domain of human CD28 receptor; and

[1] Claims 1-20 are pending, claims 8-20 have been withdrawn from consideration, and claims 3-5 stand objected to as being dependent on a rejected claim. See Appeal Brief, page 1.

(c) a transmembrane domain, wherein the transmembrane domain is disposed between the single-chain antibody and the signaling domain.

The examiner relies upon the following references:

Roberts	5,686,281	Nov.11, 1997
Eshhar et al. (Eshhar)	WO93/19163	Sep. 30, 1993

Sambrook et al. (Sambrook), Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Laboratory Press, pages 16.9 and 16.11 (1989)

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Eshhar. Those claims also stand rejected under 35 U.S.C. § 102(e) as being anticipated by Roberts. Finally, claims 1, 2, 6 and 7 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of either Eshhar or Roberts and Sambrook. After careful review of the record and consideration of the issues before us, we affirm the above rejections.

DISCUSSION

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Eshhar. As claims 1 and 2 stand and fall together, see Appeal Brief, page 3, we focus our analysis on claim 1.

According to the rejection:

a. The claims recite a recombinant polynucleotide encoding a fusion protein comprising a single chain antibody and a signaling domain of human CD28 receptor and a transmembrane domain of human CD28 between the single-chain antibody and the signaling domain.

b. Eshhar [ ] teach[es] a polynucleotide encoding a fusion protein comprising a single chain antibody and the transmembrane

> and cytoplasmic domain of CD28 (see page 7 and 8 and pages 18-19).

Examiner's Answer, page 3.

We recognize that in order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). In this case, Eshhar specifically teaches a chimeric gene that comprises a first gene segment that encodes the variable regions of the heavy and light chains of a specific antibody, linked to a flexible linker, and a second gene segment that comprises a DNA sequence encoding a partial or entire transmembrane domain, as well as the extracellular domain of a lymphocyte–triggering molecule corresponding to a lymphocyte receptor or part thereof. See Eshhar, page 7, lines 27-35. The reference teaches further that the lymphocyte-triggering molecule may be CD28. See id. at 8, lines 30-36; see also page 18, lines 9-13. Thus, we find that Eshhar teaches all of the limitations of claim 1, and the rejection is affirmed.

Appellants argue that "Eshhar does not teach a specific embodiment within the scope of the claims." See Appeal Brief, pages 3-4. Appellants assert that Eshhar provides "[a] lengthy list of lymphocyte-signalling domains . . . that includes TCR signalling components, and also other lymphocyte-signalling chains, which are listed as zeta and eta chains of CD3, the gamma chain of the FcγR and FcεR, the α, β, and γ chains of the IL-2R or any other lymphokine

receotpr [sic], CD16 α chain, D2, and CD28." Id. at 4. According to Appellants, the examples specifically disclosed by Eshhar do not reflect the breadth of the laundry list of receptor types. See id.

Appellants are essentially arguing that Eshhar has not reduced the fusion protein encoded by the polynucleotide of claim 1 to practice. A reference need not have described an actual reduction to practice of an invention, however, in order to serve as an anticipatory reference. See In re Siveramakrishnan, 673 F.2d 1383, 1384, 213 USPQ 441, 442 (CCPA 1982); In re Donohue, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985). In addition, as we have discussed above, Eshhar discloses a chimeric gene that comprises a first gene segment that encodes the variable regions of the heavy and light chains of a specific antibody, linked to a flexible linker, and a second gene segment that comprises a DNA sequence encoding a partial or entire transmembrane domain, as well as the extracellular domain of a lymphocyte–triggering molecule corresponding to a lymphocyte receptor or part thereof, and teaches that the lymphocyte triggering molecule may be CD28. We do not find that the recitation of other lymphocyte-triggering molecules that may be used in anyway rules out or teaches away from the use of CD28 as the lymphocyte-triggering molecule.

Quoting In re Arkley, 455 F.2d 586, 172 USPQ 524, 526 (CCPA 1972), appellants argue that an anticipation rejection is only proper when the reference "unequivocally disclose[s] the claimed compound or direct[s] those skilled in the art to the claimed compound without any need for picking, choosing, and

combining various disclosures not directly related to each other by the teachings of the cited reference." Appeal Brief, page 4. Appellants contend that "there is no specific description, or picture of any molecule that includes a portion of CD28," and thus the disclosure of Eshhar "is insufficient to teach a compound within the scope of the present invention, without inference or guesswork." Id. at 5.

Again, we do not agree with appellants' reasoning. A patent disclosure need not set forth a compound with such specificity such that the compound could be claimed in order to serve as an anticipatory reference under 35 U.S.C. § 102(b). See In re Schaumann, 572 F.2d 312, 317, 197 USPQ 5, 10 (CCPA 1978). We thus find that one skilled in the art, upon reading the Eshhar disclosure, would envisage the fusion protein encoded by the polynucleotide of claim 1, and "it is of no moment that each compound is not specifically named or shown by structural formula in that publication." In re Petering, 301 F.2d 676, 681-82, 133 USPQ 275, 280 (CCPA 1962); see also In re Schaumann, 572 F.2d at 317, 197 USPQ at 10 (noting that In re Arkley "should not be interpreted as establishing a new test for determining whether an invention has been described in a reference within the meaning of 35 U.S.C. § 102. . . . It was not this court's intention in Arkley to effect a change in the accepted definition of 'anticipation,' a term of art meaning 'the disclosure in the prior art of a thing substantially identical with the claimed invention.'").

Appellants argue further that Eshhar does not provide an enabling disclosure. See Appeal Brief, page 5. According to appellants, Eshhar does not provide any examples that relate to CD28 containing fusion proteins. In addition, appellants contend that the disclosure of a scFV-CD16α fusion, along with the "mere mention of CD28" is insufficient to provide an enabling disclosure, as the examiner has provided "[n]o indication of similarities between CD28 and CD16." Id. at 5. Appellants also argue "the scope of enablement which the examiner states is provided by the reference far exceeds the scope of enablement which the examiner originally acknowledged for this application." Id. at 6.

We initially note that there is no rejection for lack of enablement before us, and thus that argument is not relevant to the issues presented for appeal. Moreover, while appellants argue that the Eshhar reference is not enabling, they provide no evidence to that effect. Arguments of counsel cannot take the place of evidence in the record. See in re Scarbrough, 500 F.2d 560, 566, 182 USPQ 298, 302 (CCPA 1974); In re DeBlauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). Moreover, with respect to the argument that Eshhar does not provide an enabling disclosure, appellants do not argue or provide evidence that the nucleotide sequence of the CD28 protein was not known to the ordinary artisan, nor do they argue that the ordinary artisan would not know how to produce a CD28 fusion protein. Rather, they argue that the examiner has provided no indication of similarities between CD28 and CD16, but appellants have not set forth reasons as to why the similarity or lack of similarity of CD28

and CD16 would affect the production of a polynucleotide encoding a CD28 containing fusion protein. Therefore, we do not accept appellants' arguments that the Eshhar reference does enable the ordinary artisan to make the fusion protein encoded by the polynucleotide of claim 1.

Appellants also argue that in order for a reference to be anticipatory, it must provide a written description of the claimed invention. See Appeal Brief, page 6. According to appellants, "[o]nly by requiring that the reference also provide a written description of the invention can the patent law avoid depriving actual inventors of selected embodiments within such lists from the fruits of their labors, and avoid providing a disincentive for research and development." Id. at 7. The Eshhar reference, appellants contend, does not provide a written description of CD28 as Eshhar only mentions CD28 twice, provides no examples of fusion proteins containing CD28, does not provide a diagram of such a fusion protein or nucleotide, and also provides no sequences of a protein or polynucleotide that includes CD28. See id. at 8.

Section 102(b) of title 35 requires that "the invention was known or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent." In In re Hafner, 410 F.2d 1403, 161 USPQ 783 (CCPA1969), the court dealt with the question of whether "'[w]hat constitutes the measure of 'the invention' to determine whether what is claimed is a legally recognizable invention must also constitute 'the invention' for determining whether something lacks novelty under 35 U.S.C. 102(b).'" In re Schoenwald,

964 F.2d 1122, 1123, 22 USPQ2d 1671, 1673 (Fed. Cir. 1992) (emphasis in original). The Hafner court noted that:

> In essence, appellant is contending that a double standard should not be applied in determining the adequacy of a disclosure to anticipate under § 102, on the one hand, and to support the patentability of a claim under § 112 on the other. He feels that a disclosure adequate for the one purpose is necessarily adequate for the other but, unhappily for him, this is not so. As we shall develop, a disclosure lacking a teaching of how to use a fully disclosed compound for a specific, substantial utility or of how to use for such purpose a compound produced by a fully disclosed process is, under the present state of the law, entirely adequate to anticipate a claim to either the product or the process and, at the same time, entirely inadequate to support the allowance of such a claim.

Id. 410 F.2d at 1405, 161 USPQ at 785 (footnotes omitted); In re Schoenwald, 964 F.2d at 1123, 22 USPQ2d at 1673 (quoting the above passage from Hafner). Similarly, we do not see any requirement in section 102(b) that the disclosure provide a written description of the claimed subject matter as required by the Federal Circuit in cases such as University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (1997).

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Roberts. Again, as claims 1 and 2 stand and fall together with respect to this rejection as well, see Appeal Brief, page 3, we focus our analysis on claim 1.

According to the rejection, "Roberts teach polynucleotides that encode human CD28 cytoplasmic and transmembrane domains fused to a single-chain antibody (see column 6, lines 55-67)." Examiner's Answer, page 5.

Again we find that Roberts discloses all of the limitations of claim 1. Roberts teaches co-stimulatory chimeric DNA sequences, wherein the novel co-stimulatory chimeric DNA sequences

> comprise three domains that do no naturally exist together: (1) at least one cytoplasmic domain, which normally transduces a co-stimulatory signal resulting in activation of a messenger system, (2) at least one transmembrane domain, which crosses the outer cellular membrane, and (3) at least one extracellular receptor domain which serves to bind to a ligand, and transmit a signal to the cytoplasmic domain, resulting in a co-stimulatory signal in the host cell in which the chimeric DNA is expressed. Particularly, cytoplasmic DNA sequences of co-stimulatory molecules such as CD28 . . . cell surface receptors are employed joined to other than their natural extracellular domain by a transmembrane domain.

Id. at Col. 5, lines 18-32 (emphasis added). Roberts also provides specific examples of fusion proteins containing CD28 as the cytoplasmic domain. See Roberts, Fig. 1A, and Col. 16, Example 1.

Roberts also teaches that "[i]n particular, the extracellular domain may consist of monomeric or dimeric immunoglobulin (Ig) molecules or portions or modifications thereof." See Roberts, Col. 8, lines 47-50. Specifically, the patent teaches that

> [b]ecause association of both the heavy and light V domains are required to generate a functional antigen binding site of high affinity, in order to generate an Ig chimeric receptor with the potential to bind antigen, a total of two molecules will typically need to be introduced into the host cell. Therefore, an alternative and preferred strategy is to introduce a single molecule bearing a functional antigen binding site. This avoids the technical difficulties that may attend the introduction and coordinated expression of more than one gene construct into host cells. This "single-chain antibody" (Sab) is created by fusing together the variable domains

> of the heavy and light chains using an oligo- or polypeptide linker, thereby reconstituting an antigen binding site on a single molecule.

Id. at Col. 9, lines 18-31. Thus, we find the disclosure of Roberts anticipates the fusion protein encoded by the recombinant polynucleotide of claim 1.

Appellants reiterate their arguments with respect to Eshhar. See Appeal Brief, page 8. In addition, appellants contend that while the

> patent asserts that essentially anything with binding function can serve as the extracellular binding domain, and mentions scFv as a possibility. However, the patent provides no specific examples of scFv-containing fusions nor any specific teaching of how to make such fusions specifically. It also provides no evidence that such fusions function as asserted, nor any relationship besides binding function between scFv and the extracellular domains that are actually shown to work. Thus, this patent does not provide either an enabling disclosure or a written description of applicants; invention, but merely a generalized statement submitted to justify a generic claim.

Id. at 9.

Appellants' arguments are not convincing for the reasons set forth above to the response to argument with respect to the rejection over Eshhar. While Roberts may not specifically exemplify scFv-containing fusions, it does exemplify CD28 fusions. Moreover, the reference teaches that, in particular, the extracellular domain may consist of monomeric or dimeric immunoglobulin (Ig) molecules or portions or modifications thereof.

Finally, claims 1, 2, 6 and 7 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of either Eshhar or Roberts and Sambrook. Because we have found that Eshhar and Roberts anticipate the invention of

claim 1, and as the claims stand or fall together, see Appeal Brief, page 3, we affirm the obviousness rejections as well.

CONCLUSION

Because we find that the disclosures of Eshhar and Roberts anticipate the subject matter of claim 1, and as all of the claims stand or fall together, all of the rejections of record are affirmed.

AFFIRMED

William F. Smith
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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